



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-D-2827]

Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases.” This guidance is intended to assist sponsors in identifying the optimal dosage(s) for human prescription drugs or biological products for the treatment of oncologic diseases during clinical development prior to submitting an application for approval for a new indication and usage. This guidance does not address selection of the starting dosage for first-in-human trials nor does it address dosage optimization for radiopharmaceuticals, cellular and gene therapy products, microbiota, or cancer vaccines.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to

<https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2022-D-2827 for "Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research,

Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Mirat Shah, Center for Drug Evaluation and Research (HFD-150), Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-8547; or Stephen Ripley, Center of Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases.” Dose-finding trials (i.e., trials that include dose-escalation and dose-expansion portions with the primary objective of selecting the recommended phase II dose) for oncology drugs have historically been designed to determine the maximum tolerated dose (MTD). This paradigm was developed for cytotoxic chemotherapy drugs based on their observed steep dose-response, their limited drug target specificity, and the willingness of patients and providers to accept substantial toxicity to treat a serious, life-threatening disease. Most modern oncology drugs, such as kinase inhibitors and monoclonal antibodies, are designed to interact with a molecular pathway unique to an oncologic disease(s) (i.e., targeted therapies). These targeted therapies demonstrate different dose-response relationships compared to cytotoxic chemotherapy, such that doses below the MTD may have similar efficacy to the MTD but with fewer toxicities.

This draft guidance is intended to assist sponsors in identifying the optimal dosage(s) for human prescription drugs or biological products for the treatment of oncologic diseases during

clinical development prior to submitting an application for approval for a new indication and usage and does not address selection of the starting dosage for first-in-human trials nor does it address dosage optimization for radiopharmaceuticals, cellular and gene therapy products, microbiota, or cancer vaccines. This guidance should be considered along with the International Conference on Harmonisation (ICH) E4 guidance entitled “Dose-Response Information to Support Drug Registration” when identifying the optimal dosage(s).

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on “Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR parts 50 and 56 have been approved under OMB control number 0910-0130; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001; the collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; and the collections of information in 21 CFR part 601 have been approved under OMB control number 0910-0338.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>,

<https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: January 12, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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